FILE 'BIOTECHNO' ENTERED AT 09:19:40 ON 29 MAR 2007


FILE 'EMBASE' ENTERED AT 09:19:40 ON 29 MAR 2007


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=> s TAT (w) protein and enos
L1            8 TAT (W) PROTEIN AND ENOS

=> s l1 and HIV
L2            3 L1 AND HIV

=> d ibib abs l1 1-8
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L1 ANSWER 1 OF 8 MEDLINE on STN

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| ACCESSION NUMBER: | 2005251115 MEDLINE |
| DOCUMENT NUMBER: | PubMed ID: 15817883 |
| TITLE: | Long-term inhibition of RhoA attenuates vascular contractility by enhancing endothelial NO production in an intact rabbit mesenteric artery. |
| AUTHOR: | Shiga Noriko; Hirano Katsuya; Hirano Mayumi; Nishimura Junji; Nawata Hajime; Kanaide Hideo |
| CORPORATE SOURCE: | Division of Molecular Cardiology, Research Institute of Angiocardiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan. |
| SOURCE: | Circulation research, (2005 May 13) Vol. 96, No. 9, pp. 1014-21. Electronic Publication: 2005-04-07. Journal code: 0047103. E-ISSN: 1524-4571. |
| PUB. COUNTRY: | United States |
| DOCUMENT TYPE: | (IN VITRO) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) |
| LANGUAGE: | English |
| FILE SEGMENT: | Priority Journals |
| ENTRY MONTH: | 200510 |
| ENTRY DATE: | Entered STN: 14 May 2005 Last Updated on STN: 1 Nov 2005 Entered Medline: 31 Oct 2005 |

AB RhoA plays a critical role in regulating NO production in cultured endothelial cells. To determine its role in in situ endothelial cells, we investigated the effects of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase inhibitors and a RhoA-binding domain of Rho-kinase (RB) on vascular contractility in the isolated rabbit mesenteric artery. Ex vivo treatment of the strips with 3x10(-5) mol/L simvastatin and fluvastatin for approximately 24 to 30 hours significantly attenuated the contractile response to phenylephrine and high K+ in the presence of endothelium. The addition of N(omega)-nitro-L-arginine methyl ester and the removal of endothelium abolished the attenuation of the contractile response. The cotreatment with geranylgeranyl pyrophosphate prevented the statin-induced attenuation of the contractile response, whereas geranylgeranyl transferase inhibitor mimicked the effect of simvastatin. Treatment with simvastatin enhanced the bradykinin-induced endothelium-dependent relaxation in the mesenteric artery, whereas it had no effect on the bradykinin-induced [Ca2+]i elevation in endothelial cells of the aortic valves. Introduction of RB to the strips using a cell-penetrating peptide of Tat protein (TATHA-RB) attenuated the contractile responses in a NO-dependent manner. However, a Rac1/Cdc42-binding fragment of p21-activated protein kinase, RB without Tat peptide or TATHA-protein A had no effect. The in vivo treatment of rabbit with simvastatin and TATHA-RB attenuated the contractility in a NO-dependent manner. Simvastatin and TATHA-RB significantly upregulated eNOS

in the rabbit mesenteric artery. The present study provides the first evidence that RhoA plays a physiological role in suppressing NO production in in situ endothelial cells.

L1 ANSWER 2 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2003408195 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12947275
TITLE: Hiv Tat protein causes endothelial dysfunction in porcine coronary arteries.
AUTHOR: Paladugu Ramesh; Fu Weiping; Conklin Brian S; Lin Peter H; Lumsden Alan B; Yao Qizhi; Chen Changyi
CORPORATE SOURCE: Department of Surgery Baylor College of Medicine, Methodist Hospital, Houston, TX 77030, USA.
CONTRACT NUMBER: R01 HL60135 (NHLBI)
R01 HL61943 (NHLBI)
R01 HL65916 (NHLBI)
R01 HL72716 (NHLBI)
R21 AI49116 (NIAID)
SOURCE: Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter, (2003 Sep) Vol. 38, No. 3, pp. 549-55; discussion 555-6.
Journal code: 8407742. ISSN: 0741-5214.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 30 Aug 2003
Last Updated on STN: 26 Sep 2003
Entered Medline: 25 Sep 2003

AB PURPOSE: Human immune deficiency virus (HIV) infection is often associated with chronic diseases, including atherosclerosis. However, the molecular mechanisms are largely unknown. We examined the effect of Tat protein, an HIV regulatory protein, on endothelial function in porcine coronary arteries. METHODS: Porcine coronary arteries were dissected from nine pig hearts and cut into 5-mm ring segments, which were incubated as controls or with Tat protein (10(-7), 10(-9), 10(-11) mol/L) or Tat protein plus anti-Tat antibody, for 24 hours. Myography was performed with thromboxane A(2) analog U46619 (10 (-7) mol/L) for contraction and with graded doses of bradykinin (10(-8), 10(-7), and 10(-6) mol/L) or sodium nitroprusside (10(-5) mol/L) for relaxation. Endothelial nitric oxide synthase ( eNOS) messenger RNA was determined with reverse transcriptase polymerase chain reaction (RT-PCR), and protein levels were determined with Western blot analysis. Immunoreactivity of eNOS of treated rings was also detected. RESULTS: Endothelium-dependent vasorelaxation (10-7 mol/L of bradykinin) was significantly reduced (46.41%) in pig coronary artery rings treated with 10(-7) mol/L of Tat protein, as compared with control arteries (P <.05). Arteries treated with Tat protein plus anti-Tat antibody relaxed similarly as control arteries. There were no differences in smooth muscle contractility (U46619) or endothelium-independent vasorelaxation (sodium nitroprusside) between control and Tat protein-treated groups. RT-PCR for eNOS mRNA showed reduction in eNOS levels for Tat-treated coronary artery rings by 73%, as compared with control vessels (P <.05). Tat protein-treated vessels demonstrated substantially less eNOS protein band intensity and immunoreactivity compared with control vessels. CONCLUSIONS: Tat protein significantly decreased endothelium-dependent vasorelaxation and eNOS mRNA and protein expression in endothelial cells of porcine

coronary arteries. This study suggests that Tat protein -mediated endothelial dysfunction may be important in coronary heart disease in HIV-infected patients.

L1 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:306612 BIOSIS
DOCUMENT NUMBER: PREV200510087733
TITLE: Long-term inhibition of RhoA attenuates vascular contractility by enhancing endothelial NO production in an intact rabbit mesenteric artery.
AUTHOR(S): Shiga, Noriko; Hirano, Katsuya; Hirano, Mayumi; Nishimura, Junji; Nawata, Hajime; Kanaide, Hideo [Reprint Author]
CORPORATE SOURCE: Kyushu Univ, Grad Sch Med Sci, Res Inst Angiocardiol, Div Mol Cardiol,Higashi Ku, 3-1-1 Maidashi, Fukuoka 8128582, Japan
kanaide@molcar.med.kyushu-u.ac.jp
SOURCE: Circulation Research, (MAY 13 2005) Vol. 96, No. 9, pp. 1014-1021.
CODEN: CIRUAL. ISSN: 0009-7330.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2005
Last Updated on STN: 15 Aug 2005

AB RhoA plays a critical role in regulating NO production in cultured endothelial cells. To determine its role in in situ endothelial cells, we investigated the effects of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase inhibitors and a RhoA-binding domain of Rho-kinase (RB) on vascular contractility in the isolated rabbit mesenteric artery. Ex vivo treatment of the strips with 3 x 10(-5) mol/ L simvastatin and fluvastatin for approximate to 24 to 30 hours significantly attenuated the contractile response to phenylephrine and high K+ in the presence of endothelium. The addition of N-omega-nitro-L-arginine methyl ester and the removal of endothelium abolished the attenuation of the contractile response. The cotreatment with geranylgeranyl pyrophosphate prevented thestatin-induced attenuation of the contractile response, whereas geranylgeranyl transferase inhibitor mimicked the effect of simvastatin. Treatment with simvastatin enhanced the bradykinin-induced endothelium-dependent relaxation in the mesenteric artery, whereas it had no effect on the bradykinin-induced [Ca2+](i) elevation in endothelial cells of the aortic valves. Introduction of RB to the strips using a cell-penetrating peptide of Tat protein (TATHA-RB) attenuated the contractile responses in a NO-dependent manner. However, a Rac1/Cdc42-binding fragment of p21-activated protein kinase, RB without Tat peptide or TATHA-protein A had no effect. The in vivo treatment of rabbit with simvastatin and TATHA-RB attenuated the contractility in a NO-dependent manner. Simvastatin and TATHA-RB significantly upregulated eNOS in the rabbit mesenteric artery. The present study provides the first evidence that RhoA plays a physiological role in suppressing NO production in in situ endothelial cells.

L1 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:9480 BIOSIS
DOCUMENT NUMBER: PREV200400011829
TITLE: HIV Tat protein causes endothelial dysfunction in porcine coronary arteries.
AUTHOR(S): Paladugu, Ramesh; Fu, Weiping; Conklin, Brian S.; Lin, Peter H.; Lumsden, Alan B.; Yao, Qizhi; Chen, Changyi [Reprint Author]
CORPORATE SOURCE: Department of Surgery, Baylor College of Medicine, One Baylor Plaza, Mail stop: NAB-2010, Houston, TX, 77030, USA
jchen@bcmt.tmc.edu
SOURCE: Journal of Vascular Surgery, (September 2003) Vol. 38, No. 3, pp. 549-556. print.
ISSN: 0741-5214.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

AB Purpose: Human immune deficiency virus (HIV) infection is often associated with chronic diseases, including atherosclerosis. However, the molecular mechanisms are largely unknown. We examined the effect of Tat protein, an HIV regulatory protein, on endothelial function in porcine coronary arteries. Methods: Porcine coronary arteries were dissected from nine pig hearts and cut into 5-mm ring segments, which were incubated as controls or with Tat protein (10-7, 10-9, 10-11 mol/L) or Tat protein plus anti-Tat antibody, for 24 hours. Myography was performed with thromboxane A2 analog U46619 (10-7 mol/L) for contraction and with graded doses of bradykinin (10-8, 10-7, and 10-6 mol/L) or sodium nitroprusside (10-5 mol/L) for relaxation. Endothelial nitric oxide synthase (eNOS) messenger RNA was determined with reverse transcriptase polymerase chain reaction (RT-PCR), and protein levels were determined with Western blot analysis. Immunoreactivity of eNOS of treated rings was also detected. Results: Endothelium-dependent vasorelaxation (10-7 mol/L of bradykinin) was significantly reduced (46.41%) in pig coronary artery rings treated with 10-7 mol/L of Tat protein, as compared with control arteries ($P < .05$). Arteries treated with Tat protein plus anti-Tat antibody relaxed similarly as control arteries. There were no differences in smooth muscle contractility (U46619) or endothelium-independent vasorelaxation (sodium nitroprusside) between control and Tat protein-treated groups. RT-PCR for eNOS mRNA showed reduction in eNOS levels for Tat-treated coronary artery rings by 73%, as compared with control vessels ($P < .05$). Tat protein-treated vessels demonstrated substantially less eNOS protein band intensity and immunoreactivity compared with control vessels. Conclusions: Tat protein significantly decreased endothelium-dependent vasorelaxation and eNOS mRNA and protein expression in endothelial cells of porcine coronary arteries. This study suggests that Tat protein-mediated endothelial dysfunction may be important in coronary heart disease in HIV-infected patients.

L1 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:398440 CAPLUS
DOCUMENT NUMBER: 143:146233
TITLE: Long-Term Inhibition of RhoA Attenuates Vascular Contractility by Enhancing Endothelial NO Production in an Intact Rabbit Mesenteric Artery
AUTHOR(S): Shiga, Noriko; Hirano, Katsuya; Hirano, Mayumi; Nishimura, Junji; Nawata, Hajime; Kanaide, Hideo
CORPORATE SOURCE: Division of Molecular Cardiology, Research Institute of Angiocardiology, and Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, and Kyushu University COE Program on Lifestyle-Related Diseases, Kyushu University, Fukuoka, Japan
SOURCE: Circulation Research (2005), 96(9), 1014-1021
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RhoA plays a critical role in regulating NO production in cultured endothelial cells. To determine its role in in situ endothelial cells, we investigated the effects of 3-hydroxy-3-methyl-glutaryl CoA reductase inhibitors and a RhoA-binding domain of Rho-kinase (RB) on vascular contractility in the isolated rabbit mesenteric artery. Ex vivo treatment of the strips with 3 + 10-5 mol/L simvastatin and fluvastatin for ≈24 to 30 h significantly attenuated the contractile response to phenylephrine and

high K+ in the presence of endothelium. The addition of Nω-nitro-L-arginine Me ester and the removal of endothelium abolished the attenuation of the contractile response. The cotreatment with geranylgeranyl pyrophosphate prevented the statin-induced attenuation of the contractile response, whereas geranylgeranyl transferase inhibitor mimicked the effect of simvastatin. Treatment with simvastatin enhanced the bradykinin-induced endothelium-dependent relaxation in the mesenteric artery, whereas it had no effect on the bradykinin-induced [Ca2+]i elevation in endothelial cells of the aortic valves. Introduction of RB to the strips using a cell-penetrating peptide of Tat protein (TATHA-RB) attenuated the contractile responses in a NO-dependent manner. However, a Rac1/Cdc42-binding fragment of p21-activated protein kinase, RB without Tat peptide or TATHA-protein A had no effect. The in vivo treatment of rabbit with simvastatin and TATHA-RB attenuated the contractility in a NO-dependent manner. Simvastatin and TATHA-RB significantly upregulated eNOS in the rabbit mesenteric artery. The present study provides the first evidence that RhoA plays a physiol. role in suppressing NO production in in situ endothelial cells.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:304629 CAPLUS
DOCUMENT NUMBER: 142:349066
TITLE: Uses of endothelial nitric oxide synthase comprising TAT protein transduction domain in treatment and diagnosis of vascular diseases
INVENTOR(S): Price, Elmer M.; Laughlin, Harold; Woodman, Chris; Tanner, Miles; Sturek, Michael
PATENT ASSIGNEE(S): The Curators of the University of Missouri, USA
SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2005074448 | A1 | 20050407 | US 2004-808248 | | 20040324 |
| PRIORITY APPLN. INFO.: | | | US 2003-457136P | P | 20030324 |

AB Endothelial cells produce many factors that are involved in maintaining blood vessels. One of the best understood and most studied factor is nitric oxide (NO), which is produced by an endothelial enzyme called nitric oxide synthase (eNOS). The present invention provides a mol. designed to be delivered to the endothelium where it can reconstitute eNOS activity and restore NO production The present invention concerns the use of endothelial nitric oxide (eNOS) in the treatment and prevention of endothelial and vascular disorders. Thus, the present invention provides methods of detecting, treating and preventing diseases or disorders associated with the vasculature and denoted by reduced levels of eNOS in the endothelium, as well as a concomitant reduction in the amount of NO that can be produced.

L1 ANSWER 7 OF 8 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005362601 EMBASE
TITLE: HIV Tat protein causes endothelial dysfunction in porcine coronary arteries.
AUTHOR: Paladugu R.; Fu W.; Conklin B.S.; Lin P.H.; Lumsden A.B.; Yao Q.; Chen C.; Geary R.
CORPORATE SOURCE: Dr. C. Chen, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Mail Stop: NAB-2010, One Baylor

Plaza, Houston, TX 77030, United States. jchen@bcmt.tmc.edu

SOURCE: Journal of Vascular Surgery, (2003) Vol. 38, No. 3, pp. 549-556. .
Refs: 39
ISSN: 0741-5214 CODEN: JVSUES

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Oct 2005
Last Updated on STN: 27 Oct 2005

AB Purpose: Human immune deficiency virus (HIV) infection is often associated with chronic diseases, including atherosclerosis. However, the molecular mechanisms are largely unknown. We examined the effect of Tat protein, an HIV regulatory protein, on endothelial function in porcine coronary arteries. Methods: Porcine coronary arteries were dissected from nine pig hearts and cut into 5-mm ring segments, which were incubated as controls or with Tat protein (10(-7), 10(-9), 10(-11) mol/L) or Tat protein plus anti-Tat antibody, for 24 hours. Myography was performed with thromboxane A (2) analog U46619 (10(-7) mol/L) for contraction and with graded doses of bradykinin (10(-8), 10(-7), and 10 (-6) mol/L) or sodium nitroprusside (10(-5) mol/L) for relaxation. Endothelial nitric oxide synthase ( eNOS) messenger RNA was determined with reverse transcriptase polymerase chain reaction (RT-PCR), and protein levels were determined with Western blot analysis. Immunoreactivity of eNOS of treated rings was also detected. Results: Endothelium-dependent vasorelaxation (10(-7) mol/L of bradykinin) was significantly reduced (46.41%) in pig coronary artery rings treated with 10(-7) mol/L of Tat protein, as compared with control arteries ($P < .05$). Arteries treated with Tat protein plus anti-Tat antibody relaxed similarly as control arteries. There were no differences in smooth muscle contractility (U46619) or endothelium-independent vasorelaxation (sodium nitroprusside) between control and Tat protein-treated groups. RT-PCR for eNOS mRNA showed reduction in eNOS levels for Tat-treated coronary artery rings by 73%, as compared with control vessels ($P < .05$). Tat protein-treated vessels demonstrated substantially less eNOS protein band intensity and immunoreactivity compared with control vessels. Conclusions: Tat protein significantly decreased endothelium-dependent vasorelaxation and eNOS mRNA and protein expression in endothelial cells of porcine coronary arteries. This study suggests that Tat protein -mediated endothelial dysfunction may be important in coronary heart disease in HIV-infected patients. Copyright .COPYRGT. 2003 by The Society for Vascular Surgery.



ACCESSION NUMBER: 2005231108 EMBASE
TITLE: Long-term inhibition of RhoA attenuates vascular contractility by enhancing endothelial NO production in an intact rabbit mesenteric artery.
AUTHOR: Shiga N.; Hirano K.; Hirano M.; Nishimura J.; Nawata H.; Kanaide H.
CORPORATE SOURCE: Dr. H. Kanaide, Division of Molecular Cardiology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan. kanaide@molcar.med.kyushu-u.ac.jp
SOURCE: Circulation Research, (13 Mar 2005) Vol. 96, No. 9, pp. 1014-1021. .

Refs: 32
ISSN: 0009-7330 CODEN: CIRUAL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jun 2005
Last Updated on STN: 23 Jun 2005

AB RhoA plays a critical role in regulating NO production in cultured endothelial cells. To determine its role in in situ endothelial cells, we investigated the effects of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase inhibitors and a RhoA-binding domain of Rho-kinase (RB) on vascular contractility in the isolated rabbit mesenteric artery. Ex vivo treatment of the strips with 3x10(-5) mol/L simvastatin and fluvastatin for ≈24 to 30 hours significantly attenuated the contractile response to phenylephrine and high K(+) in the presence of endothelium. The addition of N(ω)-nitro-L-arginine methyl ester and the removal of endothelium abolished the attenuation of the contractile response. The cotreatment with geranylgeranyl pyrophosphate prevented the statin-induced attenuation of the contractile response, whereas geranylgeranyl transferase inhibitor mimicked the effect of simvastatin. Treatment with simvastatin enhanced the bradykinin-induced endothelium-dependent relaxation in the mesenteric artery, whereas it had no effect on the bradykinin-induced [Ca (2+)](i) elevation in endothelial cells of the aortic valves. Introduction of RB to the strips using a cell-penetrating peptide of Tat protein (TATHA-RB) attenuated the contractile responses in a NO-dependent manner. However, a Rac1/Cdc42-binding fragment of p21-activated protein kinase, RB without Tat peptide or TATHA-protein A had no effect. The in vivo treatment of rabbit with simvastatin and TATHA-RB attenuated the contractility in a NO-dependent manner. Simvastatin and TATHA-RB significantly upregulated eNOS in the rabbit mesenteric artery. The present study provides the first evidence that RhoA plays a physiological role in suppressing NO production in in situ endothelial cells. .COPYRGT. 2005 American Heart Association, Inc

# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 6 | TAT adj protein and enos and gene adj therapy | US-PGPUB; USPAT; DERWENT | OR | ON | 2007/03/29 09:18 |